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BY

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FROM

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES.

APRIL, 1886.

ATROPHY OF THE STOMACH,
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CLINICAL FEATURES OF PROGRESSIVE PERNICIOUS ANÆMIA.

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ALTHOUGH for many years past the attempt has been made to associate certain cases of profound anæmia with wasting and degeneration of the gastric tubules, the occurrence of a primary atrophy of the mucous membrane of the stomach is still doubted, and probably the majority of pathologists agree with the statement of Welch, in his recent article on this subject in Pepper's *System of Medicine*, "that the existence of atrophy of the stomach as a primary and independent disease has not been established."

The following interesting case is offered as a contribution toward the solution of the question:

Samuel I., white, male, æt. forty-two, was admitted to the Episcopal Hospital on June 15, 1885. Seven weeks before this date he began to complain of weakness, loss of appetite, and perverted sense of taste—"everything tasted like pepper." Dyspnœa was also a prominent symptom. On slight exertion he would be seized with vertigo, and be compelled to sit down. There is no record of hemorrhage from any part of the body. There was, and still is (at date of admission), a tendency to constipation, the bowels being moved every other day. In the autumn of 1860 he had an attack of tertian intermittent. After treating himself with domestic remedies, among which vinegar and salt seem to have occupied a foremost rank, he was cured by Peruvian bark and port wine. Twenty-four years ago he had a venereal sore, followed by two suppurating buboes, but without other secondary symptoms.

He was on the police force from 1872 to 1880, during which period and subsequently, up to December, 1884, he was in the habit of drinking freely—"twenty to thirty drinks daily," many of them before breakfast—and eating at irregular hours. After leaving the police he drove



an ice wagon, and was afterward a cab-driver. Eight years ago he had an attack of gonorrhœa. In 1876 he weighed 305 pounds, and was a prominent figure at a "fat-men's ball." His height is six feet two inches. In 1877 he began to grow thin, and continued to lose flesh at the rate of one, two, and three pounds daily. He was in the habit of weighing himself on the same scales in a shop in his district. He once during this period of rapid diminution of weight, lost seven pounds in twenty-four hours. This loss of flesh continued with intermissions for eight or nine months, until his weight was reduced to 147 pounds, when he began to regain, and in a year thereafter weighed 180 pounds. The patient's memory of the exact dates of these fluctuations in his bodily weight is not absolutely accurate, though sufficiently so for the purpose of this clinical history. He attributed his loss of flesh to indigestion. At the period referred to, he was in the habit of vomiting almost invariably after taking food, and was frequently obliged to leave the table hastily on this account. His weight at time of admission was 139 pounds.

His skin possesses the peculiar yellowish pallor that is almost pathognomonic of pernicious anæmia, and the ocular conjunctiva is of the characteristic yellow hue, which differs, however, from the tint of icterus. The palpebral conjunctiva is milky-white, apparently bloodless. The skin of the abdomen is flaccid, and easily gathered in folds by a grasp of the hand, which fact is corroborative of the patient's statement regarding his former obesity. This statement, however, is proved by the best possible evidence, that of photographs in his possession. His girth was once fifty-two inches, and is now thirty-two. The patient dates his illness from a period about eight weeks prior to his admission to hospital. It began with dizziness, nausea, palpitation of the heart, and a sense of great weakness. These symptoms have continued up to date of admission.

The results of physical examination are, for the most part, negative. The heart sounds are very feeble and distant, and unaccompanied by murmur or *bruit*. The lungs are free from any sign of disease. There is neither tenderness nor increased area of dullness on percussion over liver or spleen. There is decided tenderness over middle of sternum, and a tender spot was also found on one of the lower ribs when making percussion in the splenic region. There is no enlargement of the lymphatic glands. The tongue is exceedingly pale in the centre, with pink edges and tip, but without fur. The urine contains a minute trace of albumin; its reaction is acid; its specific gravity 1.020; it is free from sugar and bile pigment. On June 16, 17, and 18, the temperature rose above normal: on the first of these dates to 101°, and on the two latter to 102°, in the evening. After the 18th the temperature was normal, while in hospital.

June 17. First examination of blood. Number of red globules per cubic millimetre, 790,000. Proportion of white to red, 1 to 158. The percentage of red globules, as compared with the normal number (5,000,000), that is to say, the "hæmic unit," is 15.8.

The majority of the globules are larger than normal and many of them are pear-shaped and oval. Microcytes present in considerable quantity. Schultze's granule masses scantily present. The color, as tested by Gowers's hæmoglobinometer, is 16 per cent.; therefore, the amount of hæmoglobin is relatively normal. This is a cardinal feature

of pernicious anæmia. In all other forms of anæmia, the percentage of hæmoglobin is lower than that of the red globules. In pernicious anæmia, it generally equals, frequently exceeds, and has been observed by Laache to be double, that of the blood globules.

18th. An ophthalmoscopic examination was made by Dr. Albert G. Heyl, one of the ophthalmic surgeons to the hospital: "Both optic disks free from swelling, margins clear and distinct. In R. E. arteries of normal calibre, veins of increased calibre, at least double the size of arteries. A large hemorrhage, for the most part decolorized, was seen above the disk, and a more recent one upward and inward, in some places quite dark, in others of a raspberry-red. In L. E. the main upper vein was very full and inclined to be tortuous. The corresponding artery was abnormally full. A hemorrhage was seen below the disk. The media were quite clear. The condition is that of engorgement of the retinal vessels, with hemorrhages such as occur in anæmia."

24th. Number of red globules per c.m., 1,195,000. Hæmic unit, 23.9. Color, 20 per cent. No white seen. The red globules vary greatly in size and shape, being oval, pear-shaped, and generally of irregular outline. Some of them are four times the normal size. There is a moderate number of microcytes.

The date on which the patient left the hospital is not preserved, but there are notes of a visit to him at his own home on June 26th, so that his stay in hospital did not exceed two weeks.

July 2. Came to have his blood examined, walking a distance of nearly two miles. Was not fatigued, but complained of a slight "numbness" in the legs. Number of red globules per c.m., 1,215,000. No white seen. Hæmic unit, 24. Color, 28. Globules abnormally large and irregular.

6th. Patient had an attack of diarrhœa, which began the day before (Sunday), although he had felt uneasiness in bowels since Friday, and had stopped his medicine in accordance with directions. He had been taking Fowler's solution, and had reached eight drops thrice a day, when diarrhœa set in.

7th. Sent for. He had five watery stools the day before, and one large, liquid, very offensive stool to-day. During the night, about 1.30, he had a decided chill. Pulse full and bounding, 112; skin hot and perspiring slightly; temperature 103.2°. Ordered 2½ grs. quiniæ sulph. every three hours, and suppository of half a grain extract. opii aq. every three hours until diarrhœa is checked.

8th. Has had thirteen stools since 12 m. the day before, but feels decidedly better, owing to subsidence of the fever. Pulse 80; temperature 99.8°. Wishes to get up.

10th (Friday). Sitting up and looking worse. Has had forty watery, offensive stools since Tuesday morning, five between 4 and 9 A.M. None since 9, when last suppository was used.

12th. Came to have his blood examined. Not so much fatigued as when he came on July 2d, which, considering the recent attack of diarrhœa, is remarkable. Number of red globules per c.m., 1,635,000. Globules, for the most part, much larger than normal, and of irregular shapes. No white in specimen. Hæmic unit, 32.5. Color, 40.

20th. Number of red globules per c.m., 1,605,000. Globules mostly very large, some of them three times the normal size, and very irregular in shape; a few microcytes. Hæmic unit, 32. Color, 30. The count is

almost the same as the last, although the patient feels decidedly better, and walks considerable distances without fatigue, in spite of the intense heat now prevailing; the thermometer to-day reached 100° F., in the shade. His appetite is good, and the bowels are moved once daily. Ordered ferri pyrophosphat., gr. iiss *ter in die*.

Aug. 2 (Sunday). On Thursday patient came to have his blood examined, but it could not be done at that time. On his way home he drank a glass of buttermilk and soon after swallowed a plate of mock-turtle soup and a glass of lemonade. The consequence was an attack of cholera morbus the same evening. He treated himself with laudanum and blackberry brandy, and by next day the attack had ceased. On Friday he weighed 135 pounds. Number of red globules per c. m., 1,640,000. Hæmic unit, 32.8. Color, 36. Average size of corpuscles still decidedly above normal. Very few microcytes. No granule masses. Shape of globules less irregular. No white cells seen.

10th. About the same. Blood not examined. Hydroleine prescribed.

15th. Feels much better. Weighs 140 pounds. Talks of getting to work—cab-driving. Has walked a distance of two miles without fatigue during the past week. Appetite good and bowels regular. Did not take hydroleine, but, by advice of an officious friend, took elix. ferri, quiniæ, et strychniæ phosphat., instead. Number of red globules per c. m., 1,805,000. Hæmic unit, 36. Color, 32. No white seen. Patient looks very pale and ghastly.

Sept. 2. Has been working as a street-car conductor for a week, getting up at 3.30 A. M., and working until late at night. Got along very well until two days ago, when an attack of diarrhoea compelled him to stop work.

12th. Working again as car conductor. Rises at 4 A. M. and does not get to bed until one o'clock next morning. He has, therefore, if his statement is correct, only three hours in bed. "Never felt better in his life," but looks exceedingly pale and thin. No. of red globules per c. m., 1,470,000. Hæmic unit, 29.4. Color, 35.

Oct. 21. No. of red globules per c. m., 1,255,000. Hæmic unit, 25. Color, 20. White corpuscles to red as 1 to 500. Globules large and irregular. Patient complains of great weakness in legs on walking short distances. Has been continuously at work as car conductor, though not on full time.

Nov. 19. Sent for, and found him lying down though dressed. Has not worked for a month and is exceedingly feeble. Has followed no regular treatment whatever, being incorrigible in this respect. Has taken lately some pills called "tree of life," which purged him freely and reduced his little remaining strength. He complained of difficulty in passing water, and stated that some years ago he had been treated for stricture by the late Dr. Maury. Passed a No. 15 (French) catheter and drew off a little limpid urine. No blood followed passage of instrument. (About ten days later No. 21 was passed without difficulty.) His quarters are very confined and dark, and exceedingly noisy from continual passage of Pennsylvania R. R. trains almost directly overhead.

Dec. 10. Sent for late at night on account of alarming dyspnoea. When visited he was relieved, the relief having succeeded the belching of large quantities of wind.

17th. About the same. He had apparently sent to inquire whether

there was any prospect of his recovery. Ordered vin. ferri amar., ʒss, and liq. potass. arsenit., mʒiiss. *ter in die*.

21st. Worse. Diarrhœa began during the night and has weakened him considerably. This has been the invariable result of attempts to administer arsenic. The diarrhœa, which amounted to seven or eight watery stools, was checked by fifteen drops of laudanum. Ordered liquor ferri dialysat., gtt. v *ter in die*, to begin to-morrow, if diarrhœa does not return.

28th. Exceedingly pale and feeble. No conveniences at house for examination of blood. Taking ten drops of solution of dialyzed iron thrice daily.

On Jan. 5th, through the kindness of Dr. S. Weir Mitchell, he was admitted to the Summer St. Hospital. For several days before, he had been exceedingly weak, unable to sit up, and complaining of a sense of utter prostration.

10th. He lay in a semi-comatose condition, from which he could be partially roused, but was unable to recognize any person. The pulse eighty, very small, soft, and compressible, and the respirations deep and sighing.

Number of red globules per c. m., 315,000. Owing to the extremely pale tint of the blood, the color test could not be employed. The count was made at three o'clock. At half-past four, Dr. T. G. Morton injected into the left internal saphenous vein, at about the junction of the middle and lower thirds of the leg, fifteen fluidounces of a solution of sodium chloride, 100 grains to the quart of distilled water. Present: Drs. Hunt, Cantrell, T. S. K. Morton, and Orville Horwitz. Toward the close of the operation, which, it is needless to say, was performed with the greatest skill, the patient became restless, and opened his eyes, but could not reply to questions. Pulse before and after transfusion unchanged in frequency (80), but somewhat fuller after the operation. 8.30 p. m., patient in condition of heavy stupor; pupils moderately dilated; pulse extremely weak, but still 80 per minute; respiration labored and sighing, but not stertorous. Died at 12.30, four hours later.

Autopsy, eleven hours after death. Rigor mortis present. Considerable emaciation. Cicatrices on glans penis. Panniculus not more than half an inch in thickness; fat of a deep yellow color. Great pallor of skin and all organs. *Muscles* of a light red tint. In *abdominal cavity*, peritoneum smooth; small amount of a dark yellow serum; the intestines distended with gas. In *right pleura* general adhesions. *Pericardium* covered with a moderate amount of mediastinal fat; slight excess of fluid in cavity. *Heart* large, right chambers full; walls flaccid; preliminary incisions show in right auricle much pale serum, with a large yellow clot; in right ventricle a colorless clot, infiltrated with serum, closely adherent to trabeculæ and chordæ; ten ounces of a watery blood were collected from these chambers. The left chambers were nearly empty; small thin clots blocked the mitral orifice. On further dissection of the heart, walls of normal thickness; muscle very anæmic, and evidently fatty; right chamber looks dilated; valves normal. *Aorta* not atheromatous; coronary arteries healthy. *Lungs* pale, crepitant throughout; the lower lobes very cedematous, and the infiltration extends to the adhesions which exist between the lobes; frothy mucus in bronchial tubes and trachea.

Spleen is slightly enlarged, moderately firm; pulp of a deep purple-

red color; the Malpighian corpuscles not evident. *Kidneys* of normal size; capsules detach readily, surfaces a little rough; on section, cut with increased resistance; cortical portions pale; small arteries at bases of pyramids very prominent. The *suprarenal capsules* are of average size, firm; cortical portions of a deep yellow color. *Bladder* contains several ounces of clear urine.

Stomach looks natural, contains gas and about an ounce of dark fluid; pyloric orifice firmly contracted, and the ring seems thickened; cardiac orifice normal; length of organ eleven inches; breadth, when opened, eight inches. Walls not increased in thickness; at fundus two to three millimetres, at middle of anterior wall two and a half to three millimetres, and at pyloric zone, ten centimetres from the ring, eight to nine millimetres. General surface of mucosa pale; mucus covers the pyloric region; there are a few dilated venules in several places. At the fundus the mucous membrane is very thin, smooth, grayish-white in color, tough, and tears with difficulty. No trace of superficial softening. In the middle zone it has the same pale gray aspect, is smooth, and there is an entire absence of the velvet-like appearance of the healthy mucosa. About the middle of the lesser curvature there is an old cicatrix, plainly shown by four or five radiating lines. In the pyloric zone, the mucosa is more vascular and decidedly thicker. Scattered over the surface of the membrane, particularly in the central zone, are numerous small, grayish-white elevations the size of a pin's head, most of them isolated, others in groups, and contiguous ones are joined by narrow lines of tissue projecting half a millimetre above the surrounding surface. Toward the pylorus there are larger, more flattened elevations, separated from each other by shallow areas of a pale gray aspect. With a low-power lens small orifices can be seen in these flattened elevations, and here and there in the smaller nodular projections little orifices and tiny cysts can also be seen. The general surface of the mucosa as examined with a hand lens, has a smooth cuticular appearance; the thin mucosa is readily movable on the muscularis; the submucosa does not appear thickened; and, with the exception of the pyloric region, there is no thickening of the muscular coat.

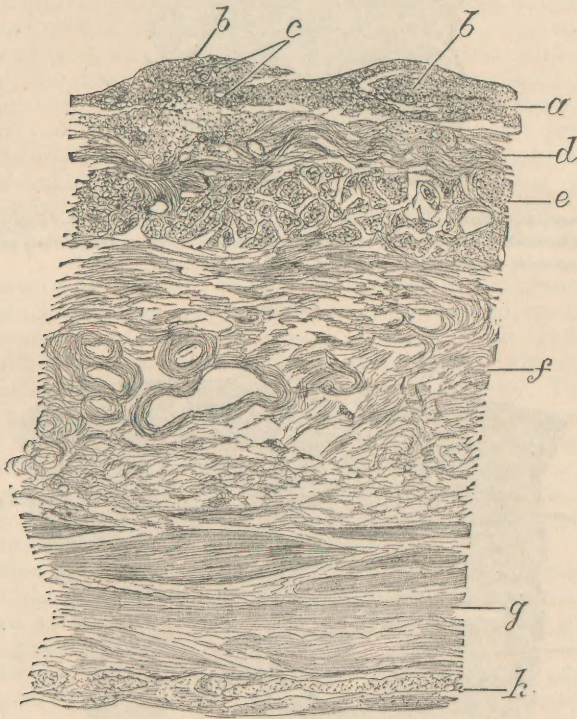
The œsophageal mucous glands are unusually distinct. *Duodenum* contains a bile-stained mucus. Bile flows freely from the orifice of the duct on compression of the gall-bladder. *Small intestines* contain a thin mucus. The walls of the jejunum look of average thickness; those of ileum thin. Peyer's gland, in the portions examined, normal. The large bowel was not opened. *Liver* looks large, is of a light yellow-brown color; capsule presents patches of thickening. Tissue cuts easily, and contains very little blood. Gall-bladder distended with pale bile. *Pancreas* very large, weighs more than 100 grammes; looks natural, lobules distinct; on section, presents a very normal appearance. *Thoracic duct* normal. The *thoracic* and *semilunar ganglia* have a natural appearance. No enlargement of the *bones*. Marrow of ribs and sternum of a deep purple-red color. That of lower portion of right tibia lymphoid, the cancellæ at the end of the bone contained fat.

Brain not examined.

HISTOLOGICAL EXAMINATION.—*Stomach*. Portions were taken from four different parts and hardened in alcohol. (1) From fundus, where the mucosa looked thinnest and had a very smooth, cuticular appearance. Entire thickness of section about 3.5 millimetres, of which

scarcely one-half is made up of the muscular coat. Neither glandular nor epithelial elements of the mucosa occur in the section, but immediately upon the muscularis mucosæ there is a narrow layer (Fig. 2, *a*) of flattened and small round cells, embedded in an indifferent matrix. In the stained preparation the nuclei of these cells are distinct, but the outlines are feebly marked. The muscularis mucosæ shows a remarkable alteration. There are two distinct layers, in the innermost of which the cells are cut longitudinally and form a prominent wavy band of fibres, which are marked even under low powers (Fig. 1, *d*, Fig. 2, *b*). From twelve to fifteen muscle cells can be counted in this band, which varies somewhat in thickness in different places. Below it, forming a much thicker and not so sharply defined layer, are the transverse fibres of the muscularis mucosæ, seen in cross-section, arranged in bundles and groups, separated by more or less connective tissue (Fig. 1, *e*, Fig. 2, *c*). They

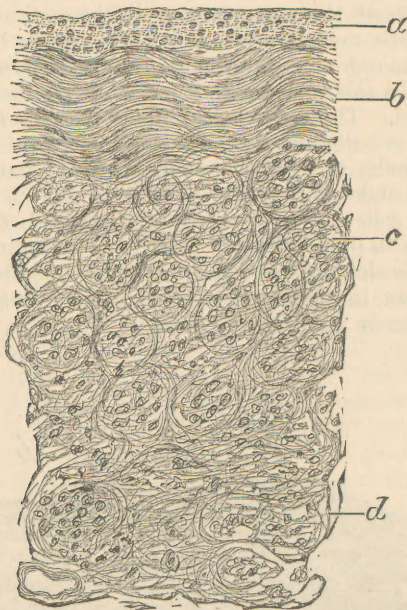
FIG. 1.



Section through mid-zone under low power, showing relations of the layers. *a*, mucous membrane with two of the nodular projections, *b, b*; *c*, remnants of tubules; *d*, muscularis mucosæ, fibres cut longitudinally; *e*, muscularis mucosæ, fibres cut transversely; *f*, submucosa; *g*, inner, *h*, outer layers of muscular coat. Low power. Ocular A. Obj. one and one-half inches.

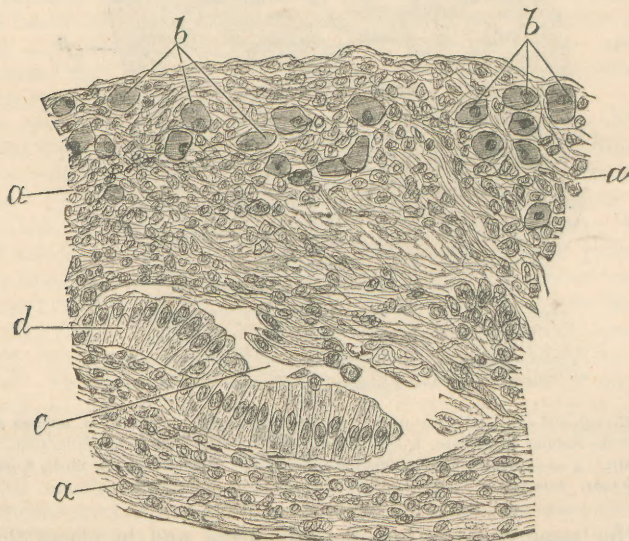
extend for some distance into the submucosa, and in places there are alternate layers of transverse and longitudinal fibres below the distinct band above mentioned. The submucosa (Fig. 1, *f*) presents coarse fibre

FIG. 2.



Section of mucosa of fundus *a*, remnants of glandular layer; *b*, inner band of muscularis mucosæ, fibres cut longitudinally; *c*, outer layer of muscularis mucosæ, fibres cut transversely and arranged in bundles; *d*, beginning of submucosa Ocular A Obj. one-fifth inch.

FIG. 3.



Portion of one of the nodular projections of mucosa, under high power. Ocular A. Obj No. 8. *a*, the small-celled infiltration; *b*, large spheroidal cells with eccentric nuclei, the remnants of the peptic cells; *c*, portion of a tubule with cylindrical epithelium; at *d*, the cells were displaced.

cells and is loosely connected to the muscular coat. The bloodvessels are numerous and large and the walls of the arteries are much thickened. The muscular layers (Fig. 1, *g* and *h*) appear normal. The muscle cells do not look so large, nor are they as well stained or well defined as those in the muscularis mucosæ.

(2) Portion of the middle zone of the stomach in which are the nodular projections. The sections, which are from three to four millimetres in thickness, present essentially the same features as those from the fundus, but the small projections offer special features of interest. They are in reality remnants, or islets, of mucous membrane left in the general atrophy, and in them can be seen fragments of gland tissue. Even on inspection of the fresh organ with a low-power lens this seemed apparent, for in these portions and nowhere else could the orifices of tubules be seen. These portions are flattened, mushroom or pear-shaped, pyramidal or even pedunculated. Three tissue elements can be seen in them: (1) a basis or matrix of small round cells (Fig. 3, *a*) which stain deeply and give a very pronounced color to these parts; (2) large rounded epithelioid cells with eccentric nuclei, resembling, though somewhat larger than the normal gland cells of the peptic tubules (Fig. 3, *b*, *b*); (3) remnants of the tubules (Fig. 3, *d*), chiefly of the uppermost portions, with columnar epithelium. In many sections these tubules are represented as empty spaces (Fig. 1, *e*) from which the cells have fallen, in others they are still present. A normal-looking tubule was not seen, only portions; in places cystic dilatation seems to have occurred. At the base of the projections the small-celled infiltration is very dense and abuts directly in the longitudinally cut band of fibres of the muscularis mucosæ. Between two of these nodules, the mucosa has the appearance described in section 1.

(3) Flattened elevations in the pyloric region 5 or 6 centimetres from the ring, which were 5 or 6 millimetres in diameter, and stood out distinctly surrounded by areas of pale gray mucosa. With the low-power lens the orifices of peptic tubules can be plainly seen. On section, the columnar epithelium of the surface is seen in a few places. The tubules are distinct, particularly in the central portion of the patches, but the amount of small-celled intertubular growth is very great, and toward the margins it becomes the preponderating tissue, and a peptic tubule is only here and there noticeable. The cells of the tubules look normal in the central portion of these elevations, but toward the periphery they can be seen in all stages of atrophic degeneration.

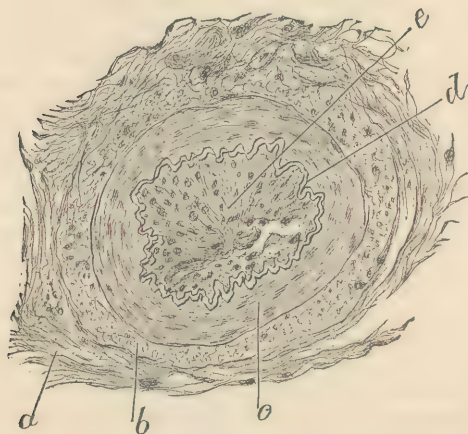
(4) Portion from the neighborhood of the pylorus. Thickness of section nearly six millimetres. Epithelium not apparent on the surfaces. The tubules are numerous and large, with normal-looking epithelium. There are groups of closely set glands, but in most places the tubules are separated by the small-cell infiltration, which in certain regions, corresponding doubtless to the interspaces between the mammillations, occupies the entire thickness. Small cysts also occur in this region. The muscularis mucosa is thicker here than in the sections described under (3).

The arteries in the submucosa presented thickened walls, particularly the muscular coat, and in almost every section vessels could be seen in process of obliteration by subintimal proliferation, as represented in Fig. 4.

Bits of the fresh mucosa from various parts were teased carefully in salt

solution. Except in the pyloric zone, no tubules or cylindrical epithelium were found. In some of the nodular projections remnants of gland tissue and a few columnar cells were seen. Gentle scrapings of the surface and the teased bits show a large number of flattened cells, unlike anything

FIG. 4.



Section of a small artery in submucosa. *a*, stroma; *b*, adventitia; *c*, muscularis; *d*, elastic lamina of intima; *e*, proliferation of subendothelial connective tissue, resulting in almost complete obliteration of the lumen of the vessel.

met with in the normal mucosa. They are irregular in shape, longer than broad, with granular protoplasm and central nuclei. The average measurements of a number gave $\frac{1}{1280}$ to $\frac{1}{858}$ of an inch in length, and $\frac{1}{2560}$ to $\frac{1}{1280}$ of an inch in breadth. Some of these are remarkably long; measurements of four gave $\frac{1}{233}$, $\frac{1}{320}$, $\frac{1}{284}$, and $\frac{1}{256}$ of an inch, and from $\frac{1}{800}$ to $\frac{1}{1000}$ of an inch in breadth. Many of the cells, particularly in the pyloric region, look like swollen glandular epithelium of the peptic follicles. Flat ribbon-like muscle cells are numerous in all the portions examined, and there is a distinct fibrous stroma thickly beset with cells. Throughout this there are in places groups of rounded, translucent bodies, resembling the amyloid corpuscles met with in degenerating tissues.

Sections of the *duodenum* show many normal-looking tubules, but here, too, the amount of intertubular tissue seems excessive. Brunner's glands look healthy.

Unfortunately, by an oversight, portions of the jejunum and ileum were not reserved for examination.

Pancreas. Cells of the acini very granular, but otherwise normal; in places there are dark brown pigment grains. The interacinous connective tissue is slightly increased.

Heart muscle very fatty, but the degeneration is unequally distributed, as is evident, indeed, macroscopically. The brown pigment granules are very abundant in many fibres.

Liver. Cells distinct, moderately fatty. Small brown-red pigment

grains very abundant both in the gland cells and in the connective tissue elements.

Kidneys. Epithelium of cortical portions swollen, and in places very fatty. The reddish pigment granules are very numerous, both in the convoluted tubes and in the epithelium of the loops of Henle, and in some of the collecting tubules.

The *bone marrow* presents the usual constituents of this tissue. There is very little fat; the marrow cells of various sizes make up the chief part, but the ordinary red corpuscles are abundant, and many of them are very large (megalocytes). Nucleated red corpuscles occur in numbers. There is no essential difference between the marrow of rib, sternum, and tibia, except that in the last-named bone the cancellæ at the end contained fat.

Sections of the *semilunar ganglia* show deeply pigmented nerve cells and an excess of connective tissue.

SUMMARY.—*Clinical.* History of drinking habits for many years. Ten years ago severe gastric symptoms with great loss of flesh. For more than nine months severe symptoms of anæmia, with nausea, occasional diarrhoea, and irregular fever. Corpuscles greatly reduced, sinking to 315,000 per cubic millimetre. Transfusion; death.

Anatomical. Extreme anæmia, with the usual fatty changes in the organs and hyperplasia of the marrow of long bones. Atrophy of mucous membrane of the stomach, with complete destruction of the secretory tubules in the larger part of the organ. Hypertrophy of the muscularis mucosæ.

REMARKS.—The patient with the foregoing clinical history presented a vivid picture of progressive pernicious anæmia. Every symptom was present in bold relief: the excessive pallor and prostration, the anæmic fever, the retinal hemorrhages, and, above all, the extreme reduction in the number of the red globules, with, at the same time, a normal *proportion* of hæmoglobin, the alterations in the size and shape of the globules (poikilocytosis), and the presence of microcytes in abnormal amount. The most prominent symptoms were those of profound gastric disturbance, due to the prolonged abuse of alcohol, and the rapid diminution of weight. In less than one year the patient lost more than one hundred and fifty pounds. This is by no means the first case of pernicious anæmia to which gastric disorder stands in causative relation. Similar cases have been reported by Fenwick,¹ Quincke,² and Nothnagel,³ through which a bright light has been thrown upon the pathology of this hitherto obscure disease, and it is for this reason that exception is now taken to the indiscriminate application of the term “idiopathic” to cases of progressive pernicious anæmia. The rapid loss of flesh may be regarded from another point of view than that of symptomatology. It is a well-attested fact that fevers, inflammatory and essential, are of more serious import in fleshy, so-called plethoric individuals, than in those of sparer habit, and, in explanation, von Recklinghausen⁴ sug-

¹ Atrophy of the Stomach, 1871.

² Deutsches Archiv für klin. Med., Bd. xxiv.

³ Volkmann's Sammlung Klin. Vorträge.

⁴ Deutsche Chirurgie, 1883, Bd. i. p. 180.

gests that the rapid absorption of fat and the products of fatty metamorphosis may give rise to a qualitative change in the composition of the blood.

The conservation of the muscular strength is also worthy of notice in this and other cases. On August 15 the patient walked two miles without fatigue, when there were less than 2,000,000 red globules per cubic millimetre. A patient of Laache, of Christiania, walked three kilometres (more than two miles), the entire distance being *up hill*, when his blood contained less than 1,000,000 globules per cubic millimetre.¹ Such facts acquire additional significance when taken in connection with the deep red color of the muscles in these cases. It would appear that the muscles in pernicious anæmia are nourished at the expense of the other tissues.

All attempts at treatment in this case were rendered nugatory by the irritable state of the intestinal tract and by the patient's wilfulness and perversity in regard to matters of diet. Leaving out the blood examinations, in which he always took a keen interest, it was impossible to secure his coöperation in any diagnostic or therapeutic procedure. Although repeatedly requested to save the urine secreted during the whole twenty-four hours, in order that its percentage of urea might be estimated, he only managed to do so once. On this occasion (June 26) the amount was 45 oz.; sp. gr., 1.012; percentage of urea, 2.05 (normal). There was no albumen.

The only special lesion in the case was the atrophy of the mucous membrane of the stomach. This was evident to the naked eye in the thin, cuticular appearance, and was abundantly confirmed by the microscopical examination, which showed that the peptic glands had been destroyed over the greater portion of the organ. The numerous small elevations which existed in the middle zone, represented areas of the mucosa less advanced in degeneration, and are comparable to the nodules of relatively normal tissue which beset the surface of a cirrhotic liver. Toward the pylorus, where the atrophy was less advanced, the various stages of the process could be traced, consisting essentially in a small-celled infiltration between the tubules, such as occurs in all forms of slow interstitial inflammation; and we may reasonably conclude that this process, extending over many years, ultimately led to the condition here described. The only other alternative is the supposition that a creeping ulceration had at one time involved the greater part of the mucosa, with the exception of the little islets of tissue already mentioned, and in healing had left the membrane in this state. The radiating cicatrix at the lesser curvature no doubt indicates that the patient had had, at one time, probably in 1877, when the gastric symptoms were so marked, an

¹ Die Anämie, S. Laache, Christiania, 1883, p. 147.

ulcer in this region, but the uniform, smooth appearance of the membrane, the absence of puckering, and the condition of the muscularis mucosæ, are not consistent with the view that there had been extensive ulcerative destruction, such as in rare cases does involve the stomach. In these instances, the process is not confined solely to the layer of tubules, but involves the muscularis mucosæ, which is infiltrated with round cells, and in healing the mucosa and submucosa are closely united to each other. Except at the site of the cicatrix, the mucous membrane was in this case freely movable on the muscular coat. The remarkable hypertrophy of the muscularis mucosæ is an associated condition not easy of explanation, but we call to mind in this connection the increase in the unstriated muscle elements in other conditions associated with irritation or degeneration, as notably in the lung of the cat affected with the nematoid parasite *Ollulanis*; and in the bronchial tubes of man in some cases of chronic bronchitis.

The recorded cases of atrophy of the stomach with clinical features of pernicious anæmia are not very numerous. Fenwick¹ describes four cases, Quincke² one, Nolen³ two, and Brabazon⁴ one; and in all of these the mucous membrane was affected without special alteration in the thickness of the walls of the stomach, or any diminution in its capacity. Nothnagel's case was one of cirrhotic contraction of the stomach and atrophy of the peptic glands, with the clinical features of pernicious anæmia. In some of these cases the histological examination was very defective, and the exact condition remains doubtful. In Fenwick's cases the interstitial connective tissue was greatly increased, and the gland tubules atrophic, but there was not the extensive destruction of the glandular layer which was so marked a feature in our case. The histological account in Nothnagel's case, by W. Müller, makes it clear that there was complete atrophy of the tubules in the entire organ, with the exception of the pyloric region. There was great thickening also of the muscularis mucosæ.

It seems natural to conclude that in the case we have described, the abuse of alcohol, extending over many years, played a part in the causation of the atrophy. Certainly he had chronic dyspepsia, and had suffered from a gastric ulcer; but while these not uncommon conditions may lead to moderate wasting of the mucous membrane, such extensive destruction of tubules is rarely seen. In the cases narrated by Fenwick there was no history of alcoholism. In connection with the extensive endarteritis of the smaller gastric vessels, and the existence of scars on the glans penis and in the groins, the possibility of a syphilitic process may be considered, but we know as yet very little of the influence of syphilis on the stomach, and the recent attempt of Gaillard⁵ to connect

¹ Loc. cit.² Loc. cit.³ Centralblatt f. d. med. Wissenschaften, Bd. xx.⁴ Brit. Med. Journal, 1878, ii.⁵ Archives Générales, January, 1886.

certain forms of gastritis with this disease cannot be regarded as in any way successful. It is quite possible, however, that the state of the small arteries may have had something to do with the production of the atrophy. We have learned of late years to connect indurative processes in other organs with arterio-sclerosis and the endarteritis of the nutritive vessels of the mucosa may really have played an important part in inducing the wasting. In a recent review of this subject, Martin¹ suggests that certain lesions of the mucosa may be due to these end-arterial changes, but acknowledges that, with regard to the stomach, the facts are as yet too few to warrant any conclusions.

To the other anatomical features of the case we do not propose to refer. The reader will doubtless have noted the identity of the conditions with those in pernicious anæmia, even to the hyperplasia of the bone marrow and the pigmentation of the cells in the organs. One point, however, is worthy of note, viz., the large size and healthy appearance of the pancreas. This organ varies greatly in size, but we regard it as certainly hypertrophied in this case, and we may see here possibly a compensatory effort to supply the defects in gastric digestion.

A careful study of this case justifies, we believe, the conclusion that a primary atrophy of the mucous membrane of the stomach does occur; and it further bears out the original suggestion of Flint, confirmed by Fenwick, Nothnagel, and others, that certain of the cases of progressive pernicious anæmia depend upon profound alterations in the gastric tubules.

For the sections and drawings we are indebted to the skill of Dr. J. P. Crozier Griffith.

¹ Revue de Médecine, January, 1886.

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